labeling of drugs (without limitation on the persons to whom the statements are made); "the circumstances surrounding the distribution of the article"; "the circumstances that the article is with the knowledge of such persons . . . offered and used for a purpose for which it is neither labeled nor advertised"; and evidence that "a manufacturer knows or has knowledge of facts that would give him notice" that a drug "is to be used" for purposes other than those for which the manufacturer offered the product.

Thus, the plain language of the regulations provides that the intended use of a product can be determined on the basis of evidence other than the promotional claims made by the manufacturer. If the Agency had meant to restrict its consideration to promotional claims exclusively, as the tobacco industry suggests, it would have written a narrow regulation expressly so providing—not the broadly written regulation it actually wrote and administers.

In effect, the tobacco industry unreasonably urges the Agency to ignore the express language of the regulation and refuse to consider any evidence of intended use other than promotional claims. The Agency disagrees with this interpretation. FDA interprets the regulation to allow the Agency to consider any relevant evidence of intent, including, as discussed in sections II.A., II.B., II.C., and II.D., above, the foreseeable and actual effects and uses of the product and the internal statements, research, and actions of the manufacturer. The Agency has for years consistently interpreted the regulation in this manner. The Agency's interpretation of its own regulations is reasonable and is entitled to "controlling weight unless it is plainly erroneous or inconsistent with the regulation." *Thomas Jefferson Univ. v. Shalala*, 114 S. Ct. 2381, 2386 (1994).

c. Judicial Decisions Authorize FDA To Consider All Evidence of Intent

The tobacco industry contends that the courts have repeatedly held that the "intended use" of a product must be based on promotional claims and that the Act does not permit FDA to exercise jurisdiction over a product as a drug or a device unless the manufacturer or vendor makes overt claims for the product in connection with its sale.

Clearly, courts have found that the vendor's claims are a relevant source of evidence establishing the intended use of a product, and FDA fully agrees with these holdings. The Agency does not, however, agree with the tobacco industry's view that the cited precedents can reasonably be read to *limit* the Agency to consider only such overt claims when determining the intended use of a product. In most of the cases cited by the tobacco industry, the relevance of other types of evidence was not at issue because the manufacturers' promotional claims were found to be sufficient to establish the intended use of the products. Thus, FDA did not need to rely on other evidence to prove the intended use of the article, and the courts were not called upon to decide the relevance of other evidence. *See, e.g., Bradley v. United States*, 264 F. 79 (5th Cir. 1920); *United States v. Nutrition Service, Inc.*, 227 F. Supp. 375, 381, 383, 386 (W.D. Pa. 1964), *aff'd*, 347 F.2d 233 (3d Cir. 1965); *United States v. An Article . . . "Sudden Change,"* 409 F.2d 734, 737 (2d Cir. 1969); *Estee Lauder, Inc. v. FDA*, 727 F. Supp. 1, 2-3 (D.D.C. 1989).

Generically, the cases relied upon by the tobacco industry represent instances in which manufacturers made drug claims for products without known drug ingredients and without known pharmacological uses—not cases where manufacturers attempted to market a product with a known drug ingredient or use without complying with the Act. *Bradley*, for instance, involved pharmaceutical claims that were made for mineral water.

In this situation, claims do have an essentially dispositive role. Pharmaceutical claims will bring the product within FDA's jurisdiction, whereas relabeling the product to eliminate these claims may, in some circumstances, remove the product from FDA's jurisdiction.

The situation is fundamentally different, however, where the product contains a known drug ingredient like nicotine and has known pharmacological uses such as addiction maintenance, sedation, and stimulation. In these cases, "[s]elf serving labels cannot be used to mask true intent." *Storage Spaces Designated Nos. "8" and "49,"* 777 F.2d. at 1366 n.5. As the Second Circuit has observed, "a fact finder should be free to pierce . . . a manufacturer's . . . misleading 'nutritional' labels to find actual therapeutic intent on the basis of objective evidence." *NNFA v. FDA*, 504 F.2d 761, 789 (2d Cir. 1974), *cert denied*, 420 U.S. 946 (1975); *accord NNFA v. Mathews*, 557 F.2d at 334 ("FDA is not bound by the manufacturer's subjective claims of intent but can find actual therapeutic intent on the basis of objective evidence.").

Contrary to the tobacco industry's assertions, numerous courts have unequivocally stated that FDA could consider evidence from "any relevant source" to establish the "intended" use of a product. The courts have enunciated a principle that defines broadly the scope of the evidence that is to be used to establish intended use. That is, the intended use is based on "labeling, promotional material, advertising *and any other relevant source*." *United States v. An Article . . . "Sudden Change,"* 409 F.2d at 739 (emphasis added); *accord NNFA v. Mathews*, 557 F.2d at 334; *Action on Smoking and Health v. Harris (ASH)*, 655 F.2d 236, 239 (D.C. Cir. 1980); *Storage Spaces Designated Nos. "8" and "49,"* 777 F.2d at 1366; *Hanson v. United States*, 417 F. Supp. 30, 35 (D. Minn.), *aff'd*, 540 F.2d 947 (8th Cir. 1976); *see also United States v. 250 Jars of U.S. Fancy Pure*

Honey, 218 F. Supp. 208, 211 (E.D. Mich. 1963) (in determining intended use, a "court is not limited to the labels on such article or to the labeling which accompanies it, but may look at all relevant sources"), *aff'd*, 344 F.2d 288 (6th Cir. 1965).[1107]

The scope of "any relevant source" is extremely broad. As one court recently held, to determine intent under this standard, the Agency may "examine a wide range of evidence, including the vendor's stated intent, actual use of the product, consumer use of the product, and product marketing." *Two Plastic Drums*, 761 F. Supp. at 72. Without any implication that these are the exclusive types of evidence, courts have construed the Act to find the types of evidence discussed below, in addition to express claims, to be "other relevant sources" of a product's intended use.

i. Pharmacological or Physical Effects.

In *United States v. Undetermined Quantities . . . "Pets Smellfree,"* 22 F.3d 235 (10th Cir. 1994), the court relied heavily on expert testimony about the physiological effects of a pharmacologically active ingredient, chlortetracycline (CTC), to establish that an animal food additive, "*Smellfree,*" was in fact a drug. Specifically, the court cited "affidavits demonstrating that the use of CTC will reduce the normal levels of bacteria in the animal's intestine and that this can affect the way the animal's body functions" to "establish[] that Smell Free is intended to affect a bodily function of animals." *Id.* at 240.

[1107] Courts have adopted a parallel approach in determining intent under similar provisions of the Act. For example, in the context of determining whether a product is "intended for export" for purposes of section 801(e)(1), 21 U.S.C. 801(e)(1), "a court must examine the manufacturer's subjective intent as well as any other evidence relating to that issue." *United States v. Various Articles of Drug, Bulk Antibiotics, etc.*, Civ. No. M-95-912, slip op. at 9 (D. Md. Jun. 6, 1996).

ii. Consumer Use.

In *ASH*, a case involving a previous FDA decision not to regulate cigarettes as drugs, the court explicitly recognized that consumer use could establish the "intended use" of a product, stating that "[w]hether evidence of consumer intent is a 'relevant source' . . . depends upon whether such evidence is strong enough to justify an inference as to the vendor's intent." 655 F.2d at 239-240; *see also NNFA v. Weinberger*, 512 F.2d 688, 703 (2d Cir. 1975) (evidence before the Agency that vitamins "were used almost exclusively for therapeutic purposes" could be a proper basis to measure intent on an objective basis); *NNFA v. Mathews*, 557 F.2d 325 (2d Cir. 1977);[1108] *United States v. 789 Cases . . . Latex Surgeons' Gloves,* 799 F. Supp. 1275, 1294-1295 (D.P.R. 1992) (intended use determined by all the facts, including "actual use"); *Two Plastic Drums*, 761 F. Supp. at 72 ("a court should examine a wide range of evidence, including . . . actual use of the product . . . ."); *United States v. Kasz Enterprises, Inc.*, 855 F. Supp. at 539 ("Objective intent can be demonstrated by, among other things . . . evidence that the vendor is aware that his product is being offered *or used* by others for a purpose for which it is neither labeled nor advertised") (emphasis added).

Several other courts have concluded that relevant "consumer use" can be defined in terms of the uses that doctors and other medical practitioners make of medical devices. *See United States v. An Article of Device . . . Toftness Radiation Detector*, 731 F.2d

[1108] The manufacturers attempt to diminish the force of the *NNFA* cases by characterizing the courts' acceptance of evidence of actual consumer use as "dictum." This argument trivializes the reality that two different panels (consisting of six different jurists) over the course of three years reviewed and—without expressing any reservations regarding its legal soundness—accepted the proposition that consumer use was relevant to determine the intended use of a product. The courts' only reservation related to the lack of record *evidentiary* support regarding the extent of consumer use. *NNFA v. Weinberger*, 512 F.2d at 703; *NNFA v. Mathews*, 557 F.2d at 335.

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1253, 1257 (7th Cir. 1984) (chiropractic instrument was a device under the Act, relying in part on testimony of manufacturers' witnesses showing how they used the article to treat patients); *United States v. 22 . . . "The Ster-o-lizer MD-200,"* 714 F.Supp. at 1165 (actual use of a sterilizer by surgeons was evidence of intended use); *United States v. An Article of Device . . . Labeled in Part: "Cameron Spitler Amblo-Syntonizer,"* 261 F. Supp. 243, 245 (D. Neb. 1966) (physician use of a product for treatment of eye ailments caused the product to be a device even in the absence of express claims by the physician or by the manufacturer in the labeling).

iii. Other Evidence.

Contrary to the contention that the phrase "intended to affect" must be read narrowly to refer only to promotional representations used in connection with the sale of the product, courts have considered a wide variety of other relevant evidence. In *American Health Products Co. v. Hayes*, for example, in addition to considering product effect and other evidence, the court found that a "starch blocking" product (known as "Starchblocker") was a drug, based in part on evidence of how the product was formulated. 574 F. Supp. 1498, 1508 (S.D. N.Y. 1983) (citing evidence that the products were "manufacture[d] . . . by a process which concentrates the antinutrient to the exclusion of components which contribute food value"). In *Toftness Radiation Detector*, in addition to considering medical use and other evidence, the court cited as evidence of intended use the financial arrangements (such as tuition and leases) through which chiropractors were trained in use of the product. 731 F.2d at 1257 n.2. In *NNFA v. Mathews*, the court noted that both the toxicity of the product, 557 F.2d at 335, and FDA experience, *id.* at 335 n.8, may be considered in determining the intended use of a product.

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With regard to the latter evidence, the court stated that FDA's "general awareness of the 'numerous and widespread' therapeutic usages" can be relied upon if part of the record. *Id.* at 335 n.8; *see also Latex Surgeons' Gloves*, 799 F. Supp. at 1295 (circumstances surrounding storage and handling of products, as well as identity of customers, are relevant to intended use).

The tobacco industry contends that the court in *United States v. Articles of Drug for Veterinary Use*, 50 F.3d 497 (8th Cir. 1995), held that documentary materials must be promotional in nature before they can be considered as evidence of intended use. The comments, however, seriously mischaracterize the facts and holding of that case. The case involved products made from colostrum (a component of breast milk) that FDA argued were subject to regulation as drugs by virtue of the pharmacological claims made by the manufacturer, not because of the product's ingredients or actual pharmacological effects. This is simply another case in which promotional claims alone were sufficient to bring under FDA's drug jurisdiction a product without established pharmacological effects or uses. This case has no relevance in determining what kind of evidence can be used to establish the intended use of a product containing a known drug ingredient with widely known pharmacological effects and uses.

Similarly, the tobacco industry mischaracterizes *United States v. . . . "Instant Alberty Food,"* 83 F. Supp. 882 (D.D.C. 1949), and *United States v. Pro-Ag, Inc.*, 796 F. Supp. 1219 (D. Minn. 1991), *aff'd*, 968 F. 2d 681 (8th Cir. 1992). These cases involved "nutritional" products that lacked any established pharmacological effects and were promoted for treating disease or affecting the structure or function of the body. Because the *sole* basis for establishing intended use was promotional claims made to consumers, the courts held that the

promotional material must ordinarily have been distributed and relied on by consumers purchasing the products. These cases are not relevant where the government is relying on evidence establishing the intended uses of products with known pharmacological effects and uses, including evidence of the actual knowledge of manufacturers who are marketing the products for those effects and uses.[1109]

Thus, as a review of the judicial precedent reveals, promotional claims are a sufficient basis for an intended use finding, but not a necessary or exclusive basis. Not only has no court ever held that a promotional claim must always be present, but numerous courts have held that a product's intended use may be determined based on evidence from "any relevant source."

d. The Agency's Administrative Precedent Supports the Agency's Consideration of More Than Promotional Claims

In administrative actions, the Agency has determined intended use on the basis of evidence other than promotional claims by the manufacturer. This administrative precedent is entitled to deference. *See Wichita and Affiliated Tribes v. Hodel*, 788 F.2d 765, 778 (D.C. Cir. 1986) ("a high level of deference [is] afforded an agency on review when the issue turns on the interpretation of the agency's own prior proclamations").

[1109] Indeed, the court in *Alberty Food* recognized that, even if the manufacturer had long since stopped distributing the literature, the government could still establish intent if it could show that the manufacturer *actually intended* the products to be used for the treatment of disease:

> it is only to the extent that the abandonment of such dissemination creates an inference that the shipper did not intend, when it shipped the drugs in interstate commerce, that they be used for the treatment of the diseases named on the booklets, that the abandonment can be said to be an effective defense. *The government might introduce evidence to show that, notwithstanding such abandonment, it was still the intention of the shipper that the drugs be used for the treatment of the diseases* mentioned in the booklets.

83 F. Supp. at 887 (emphasis added).

Several of these precedents were described in the Jurisdictional Analysis. *See* 60 FR 41527–41531. Beginning in the 1980's, for instance, FDA took enforcement actions against "caine" products that were used as imitation cocaine. These imitation cocaine products contained bulk anesthetic powders, such as lidocaine or ephedrine, and were often sold as "incense." To determine the products' intended drug use, the Agency relied upon laboratory analyses of the products, the outlets in which the products were sold (e.g., "head shops"), and "street" information that the products provide a "cheap high."[1110] *See* Jurisdictional Analysis, 60 FR 41528. Similarly, in the early 1980's, FDA started to regulate as unapproved drugs U.S. imports of *Catha edulis*, or "khat," even though the Agency did not have any information about or claims by vendors.[1111] Khat is a shrub whose leaves act as a stimulant narcotic that affects the central nervous system when chewed or used as tea. The Agency relied on evidence of khat's actual effects and widely known uses to determine that it was intended for use as a drug.

The Agency has also taken the position that including a known drug ingredient in a product and listing this ingredient on the label of the product can be sufficient to make the product a drug. Thus, the Agency has formally taken the position that any skin cream that contains a pharmacologically active level of hormones and lists the presence of hormones

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[1110] *See* memorandum from chief, prescription drug compliance branch (Aug. 4, 1982), reprinted in *Rx Drug Study Bulletin #258*; OH. FDC 64350, Case No.C-3-84-686 (S.D. Ohio 1984); FDA Administrative File for Mid-America Drug Co., regulatory letter 84-DT-12 and response; FDA Administrative File for Sam's Imports, Dearborn, MI, regulatory letter 85-DT-3 and response; FDA Administrative File for NALPAC, Ltd., Oakpark, MI, regulatory letter 85-DT-5 and response; FDA Administrative File for Tower Enterprises, Ida, MI, regulatory letter 85-DT-2 and response. In 1994, the government prosecuted Edwin and Thomas Dews in Michigan for selling a product called "Milky Trails," labeled as a room deodorizer but in fact containing lidocaine. Case No. 94 CR 20040-BC (E.D. Mich.). *See* AR (Vol. 4 Ref. 30-2).

[1111] FDA Import Alert 66-23 (Mar. 26, 1982, revised Apr. 2, 1986, and Feb. 9, 1993). *See* AR (Vol. 4 Ref. 30-1).

on the label is a drug. *See* 58 FR 47611, 47612 (Sep. 9, 1993); Drug Study Bulletin No. 67 (Mar. 28, 1994); *see also* 54 FR 40618, 40619 (Oct. 2, 1989). Similarly, FDA considers dentifrice products containing fluoride to be drugs, irrespective of whether any claims are made, because fluoride is widely accepted as an anticavity agent by the dental products industry and consumers and because fluoride affects the structure of the tooth. *See* 59 FR 6084, 6088 (Feb. 9, 1994); *see also* 50 FR 39854 (Sep. 30, 1985).

As these examples and the additional examples described in the Jurisdictional Analysis indicate, the Agency regularly looks beyond a manufacturer's express promotional claims to the likely pharmacological use and effect of a product in determining whether a product is intended to affect the structure or function of the body.

e. Policy Considerations Also Weigh Strongly in Favor of the Agency's Interpretation

Finally, policy considerations also conflict with the tobacco industry's position and weigh strongly in favor of the Agency's interpretation. The purpose of the Federal Food, Drug, and Cosmetic Act is to "safeguard the public health" and protect "consumer welfare." H. Rep. No. 2139, 75th Cong., 3d Sess. 1-2 (1938), *reprinted in* 6 Legislative History 360. The Supreme Court has recognized that "the Food, Drug and Cosmetic Act is to be given a liberal construction consistent with the Act's overriding purpose to protect the public health." *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 798 (1969). As the Court stated:

> The purposes of [the Act] thus touch . . . the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection. Regard for these purposes should infuse construction of [the Act] if it is to be treated as a working instrument of government and not merely as a collection of English words.